Pharmacological data

The preparation for the assay of the P_{2T} ($P2Y_{ADP}$ or $P2T_{AC}$) receptor agonist/antagonist activity in washed human platelets for the compounds of the invention was carried out as follows.

Human venous blood (100 ml) was divided equally between 3 tubes, each containing 3.2% trisodium citrate (4 ml) as anti-coagulant. The tubes were centrifuged for 15 minutes at 240G to obtain a platelet-rich plasma (PRP) to which 300 ng/ml prostacyclin was added to stabilize the platelets during the washing procedure. Red cell free PRP was obtained by centrifugation for 10 minutes at 125 G followed by further centrifugation for 15 minutes at 640 G. The supernatant was discarded and the platelet pellet resuspended in modified, Calcium Free Tyrode solution (10 ml) (CFT), composition: NaCl 137 mM, $NaHCO_3$ 11.9 mM, NaH_2PO_4 0.4 mM, KCl 2.7 mM, $MgCl_2$, 1.1 mM, dextrose 5.6 mM, gassed with 95% O_2/5% CO_2 and maintained at 37° C. Following addition of a further 300 ng/ml PGI_2, the pooled suspension was centrifuged once more for 15 minutes at 640 G. The supernatant was discarded and the platelets resuspended initially in 10 ml CFT with further CFT added to adjust the final platelet count to 2×10^5/ml. This final suspension was stored in a 60 ml syringe at 3° C. with air excluded. To allow recovery from PGI_2-inhibition of normal function, platelets were used in aggregation studies no sooner than 2 hours after final resuspension.

In all studies, 3 ml aliquots of platelet suspension were added to tubes containing CaCI, solution (60 μl of 50 mM solution with a final concentration of 1 mM). Human fibrinogen (Sigma, F 4883) and 8-sulphophenyltheophylline (8-SPT which was used to block any P_1-agonist activity of compounds) were added to give final concentrations of 0.2 mg/ml (60 μl of 10 mg/ml solution of clottable protein in saline) and 300 nM (10 μl of 15 mM solution in 6% glucose), respectively. Platelets or buffer as appropriate were added in a volume of 150 μl to the individual wells of a 96 well plate. All measurements were made in triplicate in platelets from each donor.

The agonist/antagonist potency was assessed as follows.

Aggregation responses in 96 well plates were measured using the change in absorbance given by the plate reader at 660 nm. Either a Bio-Tec Ceres 900C or a Dynatech MR^4 were used as the plate reader.

The absorbance of each, well in the plate was read at 660 nm to establish a baseline figure. Saline or the appropriate solution of test compound was added to each well in a volume of 10 μl to give a final concentration of 0, 0.01, 0.1, 1, 10 or 100 mM. The plate was then shaken for 5 min on an orbital shaker on setting 10 and the absorbance read at 660 nm. Aggregation at this point was indicative of agonist activity of the test compound. Saline or ADP (30 mM; 10 μl of 450 mM) was then added to each well and the plate shaken for a further 5 min before reading the absorbance again at 660 nm.

Antagonist potency was estimated as a % inhibition of the control ADP response to obtain an IC_{50}. Compounds exemplified have pIC_{50} values of more than 5.0.

The invention claimed is:

1. A compound selected from the group consisting of [1S-(1α,2α,3β(1S*,2R*),5β)]-3-[7-[2-(3,4-difluorophenyl) cyclopropyl]amino]-5-(propylthio)-3H-1,2,3-triazolo[4,5-d] pyrimidin-3-yl)-5-(2-hydroxyethoxy)-cyclopentane-1,2-diol, and pharmaceutically acceptable salts thereof.

2. The compound 1S-(1α,2α,3β(1S*,2R*),5β)]-3-[7-2-(3,4-difluorophenyl)cyclopropyl]amino]-5-(propylthio)-3H-1,2,3-triazolo[4,5-d]pyrimidin-3-yl)-5-(2-hydroxyethoxy)-cyclopentane-1,2-diol.

3. A pharmaceutical composition comprising a compound as claimed in claim **1** in combination with a pharmaceutically acceptable diluent, adjuvant and/or carrier.

4. A pharmaceutical composition comprising a compound as claimed in claim **2** in combination with a pharmaceutically acceptable diluent, adjuvant and/or carrier.

5. A method of treatment of myocardial infarction which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **1**.

6. A method of treatment of myocardial infarction which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **2**.

7. A method of treatment of thrombotic stroke which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **1**.

8. A method of treatment of thrombotic stroke which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **2**.

9. A method of treatment of transient ischaemic attacks which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **1**.

10. A method of treatment of transient ischaemic attacks which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **2**.

11. A method of treatment of stable and unstable angina which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **1**.

12. A method of treatment of stable and unstable angina which comprises administering to a person suffering therefrom a therapeutically effective amount of a compound according to claim **2**.

13. A method of inhibiting platelet aggregation in a person which comprises administering a therapeutically effective amount of a compound according to claim **1** to said person.

14. A method of inhibiting platelet aggregation in a person which comprises administering a therapeutically effective amount of a compound according to claim **2** to said person.

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